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EXAMINER
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ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,041	HERMELIN, VICTOR M.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 239-301* is/are pending in the application.

4a) Of the above claim(s) *247, 249, 252, 259, 265, 268, 277, and 282-301* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,239-246,248,250,251,253-258,260-264,266,267,269-276 and 278-281* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 239-301 are pending. Claims 282-301 are withdrawn as being drawn to a non-elected invention. Claims 247, 249, 252, 259, 265, 268, and 277 are withdrawn as being drawn to a non-elected species. **Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are under consideration in the instant office action.** Receipt and consideration of Applicants' response to the restriction/species election requirement submitted on November 29, 2006 is acknowledged. It is also noted that Applicants failed to properly indicate which claims read on the elected species. However, in favor of expediting prosecution the Examiner has set forth the following office action.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1 and 239-281) and the species elections of (1) tablets as the dosage form, (2) folic acid as a vitamin, (3) calcium as the mineral, and (4) immediate release as the method of administration in the reply filed on November 29, 2006 is acknowledged. The traversal is on the ground(s) that the Examiner has allegedly failed to provide an "appropriate explanation" of a serious search burden. This is not found persuasive because (1) the Examiner clearly set forth in the restriction/election requirement mailed on August 31, 2006 that a search of the different groups would require a search of more than 17 different class/subclasses and would thus represent a serious and undue search burden upon the Office and (2) this Examiner is only allocated 18.6 hours to handle the prosecution of a given application from start to finish. A thorough search of the 17+ class/subclasses encompassed by the three different inventions (2 methods and a composition) set forth in Applicants claims would

represent a serious search burden. It is also noted that Applicants have provided no evidence to support their assertion that a search of all the claims would be coextensive. Mere argument in the absence of evidence is unpersuasive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 282-301 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 29, 2006.

Claims 247, 249, 252, 259, 265, and 268 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 29, 2006.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademark DILANTIN® ([0020]), SINEMET® ([0020]), DEPAKOTE® ([0020]), ISMO® ([0022]), RITALIN® ([0167], [0168]-[0170], and [0173]), HYTRIN® ([0175]-[0177], CARDURA® ([0187]), FOSAMAX® ([0197]), [PROPULSID® ([0201]), ZIDOVADINE® ([0205]), PARAPLATIN® ([0218)], FLOVENT® ([0222]), FLONASE®

([0222]), LOVENOX® ([0229]), PREMARIN® ([0233]) have been noted in this application. Trademarks should be capitalized wherever these appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The invention of claims 1, 239-246, 253-258, 260-264, 270-276, 278-281 is directed to non-statutory subject matter. Applicants' claims read on the natural process of eating food. For example, a sea sponge found in a coral reef that consumes edible matter in varying amounts multiple times during a given 24-hour period inherently meets the limitations of the claims. Applicants' equation, TD(t)= CD(t) + RD(t), if applicable to a sea sponge, would inherently be met by the sea sponge's consumption of food multiple times during a given 24-hour period, because all food ingested by the sea sponge would inherently comprise either a vitamin or a mineral or a combination of both. Animals are not autotrophs (i.e. they cannot produce their own food) and thus must obtain any vitamins or minerals they need via the ingestion of food, whatever that food may be. Phrases, such as, "to provide effective therapeutic levels" and to be administered to optimize levels of the active" have been treated as desired results and not

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required method steps, because the language of these phrases indicate that these are desired outcomes.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a drug delivery regimen, which comprises an active therapeutic substance(s) selected from the group consisting of vitamins, minerals, or combinations thereof administered multiple times in a 24-hour period to humans, does not reasonably provide enablement for said method administered to any animal, wherein the claimed drug delivery regimen is not equivalent to said animal ingesting edible matter comprising vitamins, minerals, or combinations thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

An analysis based upon the Wands factors is set forth below.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997);

In re Wright 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993),. See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (230 USPQ 546, 547 (Bd Pat App Int 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Breadth of Claims

Applicants' claims are broad. Applicants claimed regimen can be applied to any animal. The specification does not define animal in any way that clearly sets forth the metes and bounds of the term and in fact states in paragraph [0056] that the term animal may refer to any animal.

Nature of the invention/State of the Prior Art

The term animal is understood to refer to any member of the kingdom *Animalia* or *Metazoa*, which includes such disparate organisms as fruit flies, amoebas, humans, sea sponges, ants, humpback whales, cobras, birds, fish, amphibians, etc. (see 10th edition of the Merriam-Webster's Collegiate Dictionary (Merriam-Webster Incorporated: Springfield, Massachusetts, 1993, pp 44). The art recognizes that animals are hetertrophs. Hetertrophs are creatures which cannot product their own food (i.e. cannot produce their own sources of carbohydrates or proteins) and must consume other organisms, such as plants, animals, or combinations thereof to satisfy their caloric needs and obtain any needed minerals and vitamins. Vitamins and minerals,

in general, are essential nutrients that cannot be synthesized by a given organism (see Merck Manual Home Edition articles entitled, "Vitamins and Minerals" and "Vitamins"). The art recognizes that there are species of animals that are not known to science and/or have thus been newly discovered (Hood, Marlowe, "'Treasure trove' of new species deep in Antarctic ocean," published online on May 16, 2007 on YAHOO® news; and Fox, Maggie, "Marine species suggest Antarctic "cradle of life", published online on May 16, 2007 on YAHOO® news). What constitutes a vitamin or mineral is dependent on the physiology and biochemistry of a given animal. Science does not know what are vitamins and minerals for all animals, especially not newly discovered animals or those yet undiscovered. The prior art recognizes that the deficiency of vitamins or minerals can result in disease, such as anemia, which can result from a deficiency of folic acid or hypocalcemia, which results when the calcium in the blood is too low and is characterized by symptoms, such as confusion, memory loss, depression, hallucinations, etc.(Merck Manual Home Edition articles entitled, "Folic Acid (folate)" and "Calcium"). The prior art also recognizes that diseases resulting from a deficiency of a given vitamin or mineral can be treated by the administration of supplements comprising said vitamin or mineral as well as other treatments specific to the etiology of a given disease condition. The art recognizes that many animals, such as sponges lack a definite nervous system, and thus are incapable of higher cognitive functions such as verbal communication or dialogue ("sponge." Encylcopaedia Britannica. 2007. Encyclopedia Britannica Online. 26 May 2007). Thus, the art recognizes that many animals are incapable of communicating what dosing regimen they may consider to be "convenient." The art also implicitly recognizes that many animals are incapable of consciously complying with a drug delivery regimen requiring the conscious decision to administer a given

dose, because these animals lack the necessary higher cognitive functions and often the necessary appendages needed to self-administer a given dose of an active substance, such as an active in the form of a tablet. Nonetheless, wherein the active substance is a vitamin, mineral, or combination thereof, the art recognizes that animals are capable of self-administering, wherein self-administration is limited to the consumption of food that inherently contains vitamins, minerals, or combinations thereof.

The prior art recognizes that upon administration of a given active substance in animals having blood that the plasma concentration of said active is increased and that after some time, t, a portion of said active substance is excreted by said animal. Subsequent administration of said active would increase the blood plasma level of the active substance (See, for example: (1) Figure 6-4 on page 115 of *Comprehensive Pharmacy Review, 4th edition*, wherein said figure was originally published in Shargel L, Yu ABC: *Applied Biopharmaceutics and Pharmacokinetics, 3rd ed.* East Norwalk, CT, Appleton & Lange, 1993, p 354; and (2) Ritschel, W. A., *Handbook of Basic Pharmacokinetics...including Clinical Applications*, 4th edition, Drug Intelligence Publications, Inc., 1992: Hamilton, IL, pp 186-193). The Examiner is unaware of any specific prior art methods of measuring the dose of active substance(s) in animals lacking blood and circulatory systems (e.g. sea sponges or amoebas) that would not require one to sacrifice said animal.

The prior art does not recognize that animals lacking higher cognitive functions would perceive a difference between "bedtime" and dinnertime (see claims 260 and 278) nor that animals lacking a stomach would suffer from gastric irritation (see claims 251 and 269).

Level of One of Ordinary Skill & Predictability/Unpredictability in the Art

The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g. M.D., Ph.D., Pharm. D. or combinations thereof). There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970).

Guidance/Working Examples

The instant specification has several working examples, wherein different active substances are administered presumably to humans, because the active substances are drugs that have been approved by the FDA and/or are commercially sold for the treatment of various diseases and conditions, which humans may have (See Examples I-XIX, on pages 80-111) of the instant specification. Examples 1-10 all specifically cite plasma profiles of the drugs in said examples in human subjects. No examples demonstrate the application of the claimed regimen in non-humans or animals extremely divergent from humans such as amoebas, sponges, worms, squids, flies, ants, etc. The working examples and guidance of the instant application are sufficiently devoid of details needed to apply the claimed regimen to any animal, including amoebas, sponges, flies, etc. that any attempt to apply Applicants' method to animals that are not human would represent an undue burden upon an ordinary skilled artisan at the time of the instant invention.

The Examiner concludes that the instant claims are a drug delivery regimen, which comprises an active therapeutic substance(s) selected from the group consisting of vitamins, minerals, or combinations thereof administered multiple times in a 24-hour period to humans, does not reasonably provide enablement for said method administered to any animal, including

newly discovered animals and undiscovered animals, and wherein the claimed drug delivery regimen is not equivalent to said animal ingesting edible matter comprising vitamins, minerals, or combinations thereof. The cited claims would thus represent an extraordinarily large undue burden on a person of ordinary skill in the art at the time of the instant invention. Especially, wherein said method is applied to animals that lack a circulatory system and/or higher cognitive abilities or when applied to newly discovered or unknown animals for which science is unaware of the dietary requirements of said animals, including what constitutes vitamins and minerals for said animals.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 239-240, 262-263, and 280-281 are indefinite because it is unclear what is a derivative of the actives recited in said claims. The term derivative is not defined in the instant specification. In paragraph [0112], Applicants states, "Derivatives, as used herein, include, without limitation, salts, alkaline salts, esters and combinations thereof," which is not a definition because it does not clearly set forth the metes and bounds of said term. The 10th edition of the Merriam-Webster's Collegiate Dictionary (Merriam-Webster Incorporated: Springfield, Massachusetts, 1993, pp 311) defines "derivative" as, "a chemical substance related

structurally to another substance and theoretically derivable from it." For example, carbon dioxide could theoretically be derived from the combustion of folic acid a vitamin. Alternatively, it is theoretically possible to obtain ^{48}Ti from the double beta decay of ^{46}Ca. Therefore, the definition of derivative in the Merriam-Webster Collegiate Dictionary does not shed light on what Applicants' intended for the meaning of a fluticasone derivative.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "bioflavonoid" in claims 240, 263, and 281 is used by the claim to mean "mineral", while the accepted meaning is "any organic compound of the group of biological aromatic compounds that includes common pigments and flavones (Merriam-Webster's Collegiate Dictionary, 10th edition, Merriam-Webster, Inc.: 1993, pp 444)." The term is indefinite because the specification does not clearly redefine the term.

Claim 241 is confusing because it is unclear what efficacy is being increased by administration of the active substance(s) in the claimed drug delivery regimen.

Claim 242 is confusing because it is unclear what total dosage is being reduced by administration of the active substance(s). It is also confusing because it is unclear how the administration of a given amount of active (i.e. a dosage) can reduce itself, because the total dosage is the sum of the doses given in a particular day. If the only doses given are those of the

active substance(s) it is unclear how the total dosage of the doses given can be anything else but the total dosage.

Claim 243 is confusing because it is unclear what side effects are being reduced; and, furthermore, it is unclear how the administration of one or more doses of a given active substance or active substances can reduce the frequency of side effects associated with said active substances. If additional steps are required to obtain the result of reduced side effects, it is unclear from the claim what these steps may be.

Claim 244 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that improve patient compliance with the drug delivery regimen.

Claim 245 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that improve convenience of administration.

Claim 1 recites the limitation "the dose amount" in line 16. There is insufficient antecedent basis for this limitation in the claim.

The remaining claims are rejected for depending upon a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCarty (U.S. Patent No. 5,776,504) in view of Ritschel (*Handbook of Basic Pharmacokinetics...including Clinical Applications*, 4th edition, Drug Intelligence Publications, Inc., 1992: Hamilton, IL, pp 186-193).

NOTE: This rejection is being made for the situation wherein the animal receiving the dosing regimen is a human.

Applicant Claims

Applicant's claim a drug delivery regimen comprising the administration to an animal of an active substance selected from the group consisting of a vitamin, mineral, or combination thereof multiple times in a 24-hour period, wherein said administration is intended to provide therapeutic effective levels of said active substance and to optimize the levels of the said active substance at the site or sites of action and is characterized by the formula TD(t)- CD(t) + RD(t), wherein TD(t) is the therapeutic dose at time t, CD is the current dose at time it, and RD is the residual dose at time t.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

McCarty teaches compositions comprising magnesium taurate for the prevention and treatment of pre-eclampsia/eclampsia for oral administration as nutritional supplements in the form of **coated or uncoated tablets**, wherein the composition may comprise excipients such as **calcium carbonate** (i.e. a source of calcium), or alternatively calcium taurate or other taurate salts of essential nutrients (title; abstract; col. 5, lines 10-16, 32-56; col. 6, lines 52-55; col. 7, lines 13-30). McCarthy teaches that **magnesium is an essential nutrient** with anti-hypertensive properties and that taurine (i.e. the source of the taurate anion) has anti-hypertensive, anti-vasopressor, anti-convulsant, hypoxia-protective, and platelet-stabilizing properties (col. 4, lines 9-11 and 38-48).

Ritschel teaches several different models that describe the drug concentration at a given time and also recognizes that after a certain period of time some drug is excreted from the animal (e.g. human) to which it is administered (see Figures 14-1 on page 187; Figure 14-2 on page 188; Figure 14-3 on page 189; Figure 14-4 on page 190; Figure 14-5 on page 191; and the text on pages 186-189).

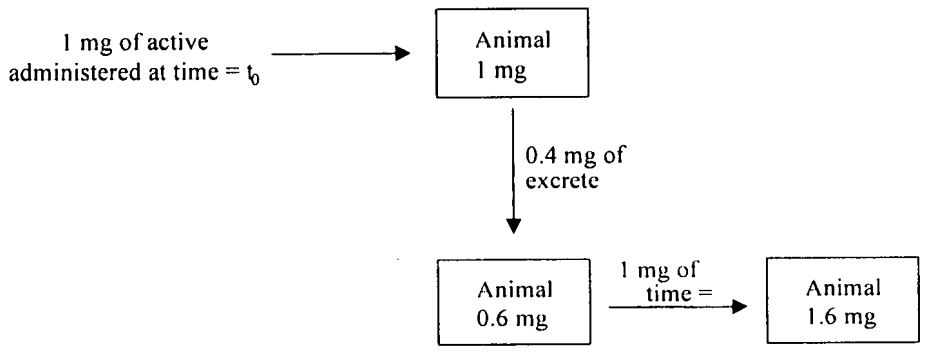
Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

McCarty lacks the teaching of (1) the formula TD(t)- CD(t) + RD(t), wherein TD(t) is the therapeutic dose at time t, CD is the current dose at time it, and RD is the residual dose at time t; (2) administration of an active substance multiple times in a 24-hour period; and (3) the administration of uneven doses at uneven time intervals and/or after bedtime and dinnertime.

These deficiencies are cured by the teachings of Ritschel and/or obviated by the teachings of Ritschel.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the instant application that the formula TD(t)- CD(t) + RD(t), wherein TD(t) is the therapeutic dose at time t, CD is the current dose at time it, and RD is the residual dose at time t is inherent to the administration of any active substance to a human or other animal comprising a circulatory system, because Applicants' formula merely represents a simplified version of the open one compartment model, which is a well-known pharmacokinetic model. An ordinary skilled artisan would have been motivated to modify the dosing regimen of a given therapeutic drug composition to provide therapeutic effective doses, because one goal of any therapeutic drug regimen is to provide therapeutically effective levels of drug. An ordinary skilled artisan would have been motivated to optimize a drug delivery regimen to provide therapeutically effective levels of a given active substance or substances, because this is the goal of any therapeutic drug delivery regimen. Active/therapeutics substances are not intended for delivery to obtain non-therapeutically effective concentrations of said substances in a given subject. Furthermore, it



would have been prima facie obvious to a person of ordinary skill in the art at the time of the instant invention that the administration of subsequent doses of an active substance within a given 24-hour period would modify the concentration of said substance in a subject as evidenced by the cartoon above. An ordinary skilled artisan would have been motivated to optimize the dosing regimen including, if necessary, such as administering uneven doses at regular or uneven intervals, such as immediately after dinner and immediately prior to bedtime, to obtain the desired result of treating a given condition with a given drug wherein treatment is effective only when therapeutically effective levels of drug are present in an animals blood. An ordinary skilled artisan would have had a reasonable expectation of success because pharmacokinetic models of drug administration are well known and established in the field of pharmacy. Applicants' data is noted and said data does not constitute any surprising or unexpected results. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paradissis et al. (U.S. Patent No. 5,776,504; IDS) or Stalker et al. (U.S. Patent No. 5,661,123; IDS) in view of Ritschel (*Handbook of Basic Pharmacokinetics...including Clinical Applications*, 4th edition, Drug Intelligence Publications, Inc., 1992: Hamilton, IL, pp 186-193).

NOTE: This rejection is being made for the situation wherein the animal receiving the dosing regimen is a human.

Applicant Claims

Applicant's claims have been described above in the instant office action.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Paradissis teaches a multi-vitamin and mineral supplement for pregnant women in the form of a **tablet** that is intended to be administered during the 1st, 2nd, and 3rd trimester of pregnancy in a specific regimen of pharmaceutically acceptable **calcium compounds**, vitamin D, **folic acid**, vitamin B12, vitamin B6, and vitamin B6, which is tailored to maximize fetal development and maternal health during each trimester of pregnancy (title; abstract; col. 3, lines 24-63; col. 5, line 45 through col. 6, line 14; col. 7, line 17 through col. 8, line 17; col. 9, lines 40-46; col. 10, lines 25-62; and claims).

Stalker teaches enteral composition for malabsorbing patients and **methods for providing nutrition to non-catabolic and moderately catabolic patients**, wherein the composition comprises protein, lipid, carbohydrate, has a caloric density of about 1,000 kcal/L, and low osmolality, wherein the composition also includes vitamins and minerals, such as **folic acid and calcium** (title, abstract; col. 1, lines 5-8; col. 2, lines 48-53; col. 3, lines 14-24, 32-63; col. 3, line 64 through col. 4, line 55; col. 5, line 58 through col. 6, line 45; claims).

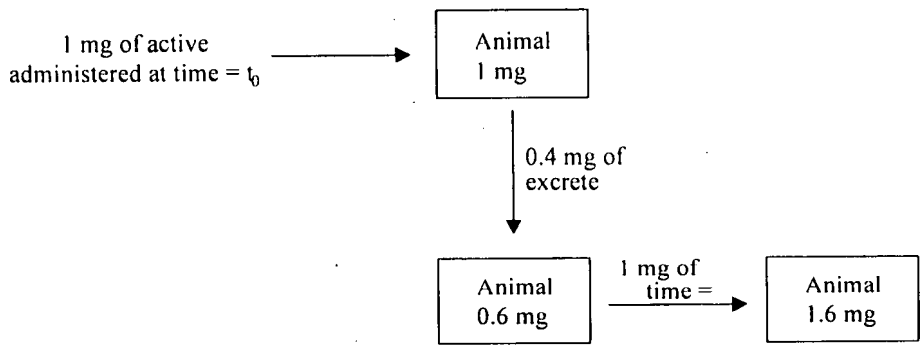
The teachings of Ritschel were set forth above in the instant office action.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Paradissis lacks the teaching of (1) the formula TD(t)- CD(t) + RD(t), wherein TD(t) is the therapeutic dose at time t, CD is the current dose at time it, and RD is the residual dose at time t; (2) administration of an active substance multiple times in a 24-hour period; and (3) the administration of uneven doses at uneven time intervals and/or after bedtime and dinnertime. These deficiencies are cured by the teachings of Ritschel and/or obviated by the teachings of Ritschel.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the instant application that the formula TD(t)- CD(t) + RD(t), wherein TD(t) is the therapeutic dose at time t, CD is the current dose at time it, and RD is the residual dose at time t is inherent to the administration of any active substance to a human or other animal comprising a circulatory system, because Applicants' formula merely represents a simplified version of the open one compartment model, which is a well-known pharmacokinetic model. An ordinary skilled artisan would have been motivated to modify the dosing regimen of a given therapeutic drug composition to provide therapeutic effective doses, because one goal of any therapeutic drug regimen is to provide therapeutically effective levels of drug. An ordinary skilled artisan would have been motivated to optimize a drug delivery regimen to provide therapeutically effective



levels of a given active substance or substances, because this is the goal of any therapeutic drug delivery regimen. Active/therapeutics substances are not intended for delivery to obtain non-therapeutically effective concentrations of said substances in a given subject. Furthermore, it would have been prima facie obvious to a person of ordinary skill in the art at the time of the instant invention that the administration of subsequent doses of an active substance within a given 24-hour period would modify the concentration of said substance in a subject as evidenced by the cartoon above. An ordinary skilled artisan would have been motivated to optimize the dosing regimen including, if necessary, such as administering uneven doses at regular or uneven intervals, such as immediately after dinner and immediately prior to bedtime, to obtain the desired result of treating a given condition with a given drug wherein treatment is effective only when therapeutically effective levels of drug are present in an animals blood. An ordinary skilled artisan would have had a reasonable expectation of success because pharmacokinetic models of drug administration are well known and established in the field of pharmacy. Applicants' data is noted and said data does not constitute any surprising or unexpected results. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-7, 10, 13-17, and 19-40 of U.S. Patent No. 5,945,123 (USPN '123). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are obvious variants of the cited claims of USPN '123. Independent claim 1 of the instant application claims a drug delivery regimen comprising an active therapeutic substance(s) selected from the group consisting of vitamins, minerals, and combinations thereof administered multiple times during at least a 24-hour period of time to provide effective therapeutic levels of the active substance at a site or sites of action in an animal characterized by the formula TD(t)- CD(t) + RD(t), wherein TD(t) is the therapeutic dose at time t, CD is the current dose at time it, and RD is the residual dose at time t. Independent claim 1 of USPN '123 is almost verbatim with independent claim 1 of the instant application, including the same equation, wherein the primary difference being that claim 1 of USPN '523 does not specify that the active substance is selected from a vitamin, mineral, or

combination thereof. However, it is noted that USPN '523 defines active therapeutic substance to include vitamins or minerals (col. 8, lines 32-44). The dependent claims of both the instant application and USPN '523 recite the same or substantially similar limitations. Therefore, the Examiner concludes that claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are prima facie obvious over claims 1-3, 5-7, 10, 13-17, and 19-40 of U.S. Patent No. 5,945,123 (USPN '123).

Claims 1 and 248 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,214,379 (USPN '379). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are obvious variants of the cited claims of USPN '379. Claim 1 of the instant application has been described above in the instant office action. Dependent claim 248 of the instant application, which depends from claim 1 states that the active therapeutic substance is administered in one or more dosage form(s) independently selected from the group consisting of liquid, solution, suspension, emulsion, tablet, multi-layer tablet, capsule, gelatin capsule, caplet, lozenge, chewable lozenge, bead, powder, granules, dispersible granules, cachets, douche, suppository, cream, topical, inhalant, patch, particle inhalant, implant, ingestible, injectable, or infusion. Claim 1 of USPN '379 claims a drug delivery regimen, which comprises: an active therapeutic substance administered during at least one 24 hour period of time to provide effective therapeutic levels of the active therapeutic substance at a site of action in an animal over said period, wherein each individual dose is independently adjusted to be administered to optimize levels of the active therapeutic substance

at the site of action for maximum efficacy, and wherein the dose amount at each administration is independently determined by the formula TD(t)=CD(t)+RD(t), where t is the time at which the dose is to be administered, TD (therapeutic dose) is the therapeutically effective dose at time (t), CD (current dose) is the dose to be administered at time (t), and RD (residual dose) is the amount of active therapeutic substance remaining from the previous dose administration; wherein the active therapeutic substance is administered in one or more dosage form(s) independently selected from the group consisting of liquid, solution, suspension, emulsion, tablet, multi-layer tablet, capsule, gelatin capsule, caplet, lozenge, chewable lozenge, bead, powder, granules, dispersible granules, cachets, douche, suppository, cream, topical, inhalant, patch, particle inhalant, implant, ingestible, injectable, or infusion; and wherein the active therapeutic substance is administered in uneven doses.

Conclusion

Claims 1, 239-246, 248, 250-251, 253-258, 260-264, 266-267, 269, 270-276, and 278-281 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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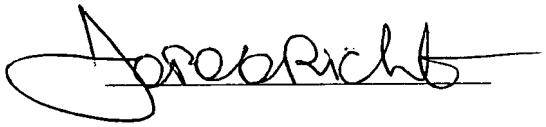

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